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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/837,344	04/19/2001	Claudine Guerin-Marchand	010830-116	2865

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EXAMINER

MINNIFIELD, NITA M

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 07/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/837,344

Applicant(s)

GUERIN-MARCHAND ET AL

Examiner

N. M. Minnifield

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 March 2004.
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 27-39 is/are pending in the application.
4a) Of the above claim(s) 27-30, 33, 34 and 38 is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 31, 32, 35-37 and 39 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 2 sheets
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.

- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicants' amendment filed March 12, 2004 is acknowledged and has been entered. Claims 1-26 have been canceled. Claim 31 has been amended. New claim 39 has been added. Claims 31, 32, 35-37 and 39 are now pending and being examined in the present application. All rejections have been withdrawn in view Applicants' amendment to the claims and/or comments with the exception of those discussed below.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. This application contains claims 27-30, 33, 34 and 38 are drawn to an invention nonelected with traverse in the reply filed in Paper No. 13. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.
4. Claims 36 and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a vaccine composition directed against malaria comprising a molecule having one or more peptide sequences bearing all or part of

one or more T epitopes resulting from the infectious activity of *P. falciparum* in the hepatic cells. Claim 37 also recites that the T epitope is selected from the group of an amino acid sequence of SEQ ID NOS: 39-42, an amino acid sequence of SEQ ID NOS: 43-46 and amino acid sequence of SEQ ID NO. 19. SEQ ID NO: 41 is the selected species.

The specification at page 25 sets forth the Construction of Genomic DNA Library and page 26 sets forth Immunological Screening of Bank. The specification does not enable a vaccine composition directed against malaria comprising a molecule having one or more peptide sequences bearing all or part of one or more T epitopes resulting from the infectious activity of *P. falciparum* in the hepatic cells.

The state of the art indicates that at present there are no vaccines that protect against malaria. Kurtis et al 2001 states that a vaccine is urgently needed to stem the global resurgence of *P. falciparum* malaria; LSA-1 is one of a few proteins known to be expressed by liver-stage parasites, holds particular promise as a vaccine (abstract). Kurtis et al 2001 states that despite "important advances, such as the circumsporozoite protein (CSP)-based vaccine called RTS,S, the goal of a safe and broadly effective malaria vaccine remains unfulfilled. The parasite's complex life-cycle offers several targets for intervention in the human host and the mosquito vector and vaccines against sporozoite, intrahepatic, blood and sexual stages of the parasite are currently in development." (p. 219, col. 1). As of 2001, there is no effective vaccine that comprises the LSA either alone or in combination with other malaria proteins. Further, because LSA is a liver specific antigen, investigation of its immunological significance is restricted to human studies because no homologue in mouse or non-human primate malarias has been

identified (p.219, col. 1). Others such as Taylor-Robinson et al 2001 have also indicated that LSA-1 may be a good candidate for a vaccine, but no vaccine has been produced that has been shown to be effective (see also Joshi et al 2000, Kurtis et al 1999, Cox, 1992). Shi et al, 1999 indicate that a multicomponent, multistage malaria vaccine can induce immune responses that inhibit parasite development at multiple stages. The rationale and approach used in the development of a multicomponent *P. falciparum* vaccine will be useful in the development of a multispecies human malaria vaccine and vaccines against other infectious diseases (see abstract). “Although studies of immunogenicity and the results of *in vitro* protection experiments have been promising for many of the single stage-specific vaccine candidate antigens, the test of *in vivo* protection has not always been satisfactory. There is consensus, however, that a highly effective malaria vaccine would require a combination of key antigens and/or epitopes from different stages of the life cycle and that induction of both humoral and cellular immunity is required for optimal efficacy. Such a multicomponent malaria vaccine would also circumvent the problems associated with host genetic restriction and antigenic variability in the case of single antigen-based vaccines.” (Shi et al, 1999, p. 1615, paragraph bridging cols. 1-2). Shi et al 1999 also indicates that multiple protective immune responses against multiple antigens from different stages will be needed to protect against malaria (p. 1618, col. 2). “Although a single-antigen and/or stage-specific vaccine could provide protection against infections, there are several reasons to advocate a multivalent, multistage malaria vaccine. A major concern with a single antigen-based vaccine is that an antigenic variant population of the parasite not recognized by the vaccine will cause infection (with heterologous parasites) and cause disease.” (see p. 1618-1619).

In view of the fact that the specification does not set forth any enablement with regard to direction or guidance and the absence of working examples for the claimed vaccine composition, and the fact that the state of the art teaches that there are no single antigen or stage specific vaccines (i.e. LSA only) against malaria and the unpredictability and difficulty in obtaining an effective vaccine directed against malaria comprising a molecule having one or more peptide sequences bearing all or part of one or more T epitopes resulting from the infectious activity of *P.*

falciparum in the hepatic cells there would be undue experimentation necessary for a person of skill in the art to practice the claimed invention.

5. Claims 31, 35, 36 and 39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6319502. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the patent and pending application claim and/or disclose a polypeptide comprising at least one T epitope or B epitope from a liver-stage specific protein produce by *P. falciparum*, and compositions comprising the polypeptide.

This rejection is maintained for the reasons of record. It is noted that Applicants have requested that this rejection be held in abeyance until there is allowable subject; at that time Applicants will file a terminal disclaimer.

6. Claims 31, 35 and 36 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 and 7 of U.S. Patent No. 5599542. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the patent and pending

application claim and/or disclose a polypeptide comprising at least one T epitope or B epitope from a liver-stage specific protein produce by *P. falciparum*, and compositions comprising the polypeptide.

The rejection is maintained for the reasons of record. Applicant's arguments filed March 12, 2004 have been fully considered but they are not persuasive. It is noted that Applicants are arguing limitations and characteristics that are not recited in either the pending claims or the claims of US Patent No. 5599542.

7. Claims 31, 35, 36 and 39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6270771. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the patent and pending application claim and/or disclose a polypeptide comprising at least one T epitope or B epitope from a liver-stage specific protein produce by *P. falciparum*, and compositions comprising the polypeptide.

This rejection is maintained for the reasons of record. It is noted that Applicants have requested that this rejection be held in abeyance until there is allowable subject; at that time Applicants will file a terminal disclaimer.

8. Claims 31, 32, 35-37 and 39 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 and 25 of copending Application No. 09/900963. Although the conflicting claims are not identical, they are not patentably distinct from each other because both pending applications claim and/or disclose a polypeptide comprising at least one T epitope or B epitope from a liver-stage specific protein produce by *P.*

falciparum, as well as vaccine compositions comprising a polypeptide comprising at least one T epitope or B epitope from a liver-stage specific protein produce by *P. falciparum*.

This rejection is maintained for the reasons of record. It is noted that Applicants have requested that this rejection be held in abeyance until there is allowable subject; at that time Applicants will file a terminal disclaimer.

9. Claims 31, 35, 36 and 39 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Guerin-Marchand et al 1987 (Nature, 329/6135:164-167).

The claims are directed to a polypeptide comprising at least on T epitope or B epitope from a liver-stage specific produced by a *P. falciparum* and a composition comprising said polypeptide comprising at least one T epitope or at least one B epitope from a liver-stage specific produced by a *P. falciparum*.

Guerin-Marchand et al disclose polypeptides that comprise a single 17 amino acid repeat that has at least one epitope and that the protein is a liver-stage specific antigen (abstract).

It is noted that the recitation of “vaccine” in claim 36 is viewed as intended use. The recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

Since the Patent Office does not have the facilities for examining and comparing applicants' polypeptides with the polypeptides of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed polypeptides and the polypeptides of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

The rejection is maintained for the reasons of record. Applicant's arguments filed March 12, 2004 have been fully considered but they are not persuasive. Applicants have asserted that Guerin-Marchand et al. disclose a liver-stage specific antigen characterized by gene cloning. More specifically a clone DG307 contained 196 base pairs composed entirely of a 51-bp repeat sequence. A synthetic peptide having part of the repeat sequence: EQQSDLEQERLAKEKLQ was synthesized and its immunogenicity was examined. It was concluded that this 17 amino acid repeat carries at least one epitope corresponding to an antibody in human sera. It is noted that this is what the claims recite.

Applicants have argued that Guerin-Marchand et al. fail to disclose a purified polypeptide comprising at least one epitope from a liver-stage protein produced by *P. falciparum* or additionally containing a B epitope. Neither T nor B epitopes are present on the antigens described in this reference, and that Guerin-Marchand et al. do not teach, either expressly or inherently, the claimed invention. However, it is noted that the prior art reference discloses that the three fusion proteins were found to be heat-stable as the LSA epitopes remained antigenic (see p. 165, col. 1). Further, Guerin-Marchand et al disclose that "...the reaction of the synthetic peptide with the serum used in the initial screening, together with its

reaction with ten other African sera indicate that a single 17 amino-acid repeat carries at least one epitope corresponding to an antibody specificity in human sera. The 17-amino-acid repeat described here is the first such reported for a malaria antigen. As repeated epitopes have been described for several *P. falciparum* antigens it is not surprising that LSA, which is immunogenic in humans, also possesses repeated structures. Computer analysis predicts that, in contrast to the CS protein, the LSA repeat with seven or eight charged amino acids may assume a helical structure. The observation that the amino-acid sequence is more highly conserved than the DNA sequence argues for a functional or structural role for these repeats. Finally the above results, obtained using a novel approach to a poorly accessible stage, provide the first data on the structure of a protein specific for the liver stage of development of *P. falciparum*. Availability of recombinant antigens, synthetic peptides and the corresponding antibodies now provide a way to evaluate the role and biological function of this stage-specific protein.” (see p. 167, col. 1).

10. No claims are allowed.

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


N. M. Minnifield

Primary Examiner

Art Unit 1645

NMM

July 8, 2004